

APR 17 2008

Appl. No. 10/749,119

Atty Docket No.: 286336.152US1/NOR-013CP2

Response to Office Action of 11/01/07

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-18. (Cancelled)

Claim 19. (Currently Amended): A method for ~~inducing~~ increasing tolerance in a patient to a graft from a MHC-mismatched donor, comprising:

depleting T cells of the patient;

reactivating the thymus of the patient; [[and]]

administering cells from the MHC-mismatched donor to the patient, the cells being selected from the group consisting of stem cells, progenitor cells, dendritic cells, and combinations thereof[[,]]; and

providing the graft from the MHC-mismatched donor to the patient,

wherein the patient has an increased tolerance to the graft compared to an untreated patient.

Claim 20. (Previously Presented): The method of claim 19, wherein the thymus of the patient has been at least in part atrophied before it is reactivated.

Claim 21. (Withdrawn): The method of claim 20, wherein the patient has a disease that at least in part atrophied the thymus of the patient.

Claim 22. (Withdrawn): The method of claim 20, wherein the patient has had a treatment of a disease that at least in part atrophied the thymus of the patient.

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Claim 23. (Previously Presented): The method of claim 19, wherein the thymus is reactivated by disruption of sex steroid-mediated signaling to the thymus.

Claim 24. (Withdrawn): The method of claim 22, wherein the treatment of the disease is immunosuppression, chemotherapy, or radiation treatment.

Claim 25. (Previously Presented): The method of claim 19, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

Claim 26. (Withdrawn): The method of claim 19, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

Claim 27. (Cancelled)

Claim 28. (Previously Presented): The method of claim 25, wherein the cells are hematopoietic stem cells.

Claim 29. (Previously Presented): The method of claim 28, wherein the hematopoietic stem cells are CD34⁺.

Claim 30. (Previously Presented): The method of claim 19, wherein the cells are administered when the thymus begins to reactivate.

Claim 31. (Previously Presented): The method of claim 23, wherein the cells are administered at the time disruption of sex steroid mediated-signaling to the thymus is begun.

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Claim 32. (Withdrawn): The method of claim 23, wherein the sex steroid-mediated signaling to the thymus is disrupted by surgical castration.

Claim 33. (Withdrawn): The method of claim 23, wherein the sex steroid-mediated signaling to the thymus is disrupted by chemical castration.

Claim 34. (Previously Presented): The method of claim 23, wherein the sex steroid-mediated signaling to the thymus is disrupted by administration of a pharmaceutical.

Claim 35. (Currently Amended): The method of claim 34, wherein the pharmaceutical is selected from the group consisting of Luteinizing Hormone Releasing Hormone (LHRH) ~~LHRH~~ agonists, LHRH antagonists, anti-LHRH vaccines, anti-androgens, anti-estrogens, Selective Estrogen Receptor Modulators (SERMs) ~~SERMs~~, Selective Androgen Receptor Modulators (SARMs) ~~SARMs~~, Selective Progesterone Response Modulators (SPRMs) ~~SPRMs~~, Estrogen Receptor Downregulators (ERDs) ~~ERDs~~, aromatase inhibitors, anti-progestogens, Dioxalan derivatives, and combinations thereof.

Claim 36. (Currently Amended): The method of claim 35, wherein the LHRH agonists are selected from the group consisting of Goserelin, Leuprolide, ~~LUPRON~~TM, Triptorelin, Meterelin, Buserelin, Histrelin, Nafarelin, Lutrelin, Leuprorelin, Deslorelin, ~~CYSTORELIN~~TM, ~~DECAPEPTYLY~~TM, Gonadorelin, and combinations thereof.

Claim 37. (Withdrawn): The method of claim 35, wherein the LHRH antagonists are selected from the group consisting of Abarelix, Cetrorelix, and combinations thereof.

Claim 38. (Previously Presented): The method of claim 19, further comprising administering at least one cytokine, at least one growth factor, or a combination of at least one cytokine and at least one growth factor to the patient.

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Claim 39. (Previously Presented): The method of claim 38, wherein the cytokine is selected from the group consisting of Interleukin 2 (IL-2), Interleukin 7 (IL-7), Interleukin 15 (IL-15), and combinations thereof.

Claim 40. (Previously Presented): The method of claim 38, wherein the growth factor is selected from the group consisting of a member of the epithelial growth factor family, a member of the fibroblast growth factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), insulin-like growth factor-1 (IGF-1), a thyroid hormone, a growth hormone, and combinations thereof.

Claim 41. (Cancelled)

Claim 42. (Currently Amended): A kit for ~~the improvement of graft acceptance~~ improving graft tolerance in a patient, the kit comprising:
an LHRH analog; and
cells from the donor of the graft, wherein the cells are selected from the group consisting of stem cells, progenitor cells, dendritic cells and combinations thereof.

Claim 43. (Previously Presented): The kit of claim 42, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

Claim 44. (Withdrawn): The kit of claim 42, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

Claim 45. (Cancelled)

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Claim 46. (Previously Presented): The kit of claim 42, wherein the LHRH analog is selected from the group consisting of a LHRH agonist, a LHRH antagonist, and combinations thereof.

Claim 47. (Previously Presented): The kit of claim 42, further comprising a cytokine, a growth factor, or a combination of a cytokine and a growth factor.

Claim 48. (Previously Presented): The kit of claim 47, wherein the cytokine is selected from the group consisting of Interleukin 2 (IL-2), Interleukin 7 (IL-7), Interleukin 15 (IL-15), and combinations thereof.

Claim 49. (Previously Presented): The kit of claim 47, wherein the growth factor is selected from the group consisting of a member of the epithelial growth factor family, a member of the fibroblast growth factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), insulin-like growth factor-1 (IGF-1), a thyroid hormone, a growth hormones, and combinations thereof.

Claims 50-52. (Cancelled)

Claim 53. (Withdrawn): A method for enhancing transplantation of donor hematopoietic stem cells into the thymus of a recipient patient, comprising:

depleting the T cells of the patient;

reactivating the thymus of the patient; and

transplanting donor hematopoietic stem cells to the patient,

wherein uptake of the donor hematopoietic stem cells into the patient's thymus is enhanced as compared to the uptake that would have otherwise occurred in a patient prior to thymus reactivation.

Claim 54. (Cancelled)

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Claim 55. (Previously Presented): The method of claim 19, wherein the patient is post-pubertal.

Claim 56. (Withdrawn): The method of claim 23, wherein the sex steroid-mediated signaling to the thymus is disrupted by lowering the level of a sex steroid hormone.

Claim 57. (Previously Presented): The method of claim 19, further comprising the step of minor myeloablation or full myeloablation.

Claim 58. (Previously Presented): The method of claim 19, wherein reactivating the thymus of the patient increases the uptake of cells into the thymus.

Claim 59. (Previously Presented): The method of claim 19, wherein the patient is immunosuppressed.

Claim 60. (Previously Presented): The method of claim 19, where the cells from the mismatched donor are genetically modified.

Claim 61. (Withdrawn): The method of claim 23, wherein the T cell depletion and disruption of sex-steroid-mediated signaling are begun at substantially the same time.

Claim 62. (Previously Presented): The method of claim 23, wherein the T cells are depleted before administration of cells from the mismatched donor to the patient.

Claim 63. (Withdrawn): The method of claim 23, wherein the disruption of sex-steroid mediated signaling is begun before T cell depletion and administration of cells.

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Claim 64. (Previously Presented): The method of claim 19, wherein the method results in the generation of a chimera selected from the group consisting of a chimeric thymus, chimeric hemopoietic cells, chimeric lymphoid cells, chimeric T cells, chimeric B cells, chimeric dendritic cells, a chimeric lymphoid organ, and any combination thereof.

Claim 65. (Canceled)

Claim 66. (Currently Amended): A method for ~~inducing~~ increasing tolerance in a patient to a graft from a MHC-mismatched donor, comprising:

depleting T cells of the patient;

reactivating the thymus of the patient; [[and]]

administering cells having the same histocompatibility as that of the

MHC-mismatched donor to the patient, the cells being selected from the group consisting of stem cells, progenitor cells, dendritic cells, and combinations thereof,]; and

providing the graft from the MHC-mismatched donor to the patient,

wherein the patient has an increased tolerance to the graft compared to an untreated patient.

Claim 67. (Withdrawn): A method for inducing tolerance in a patient to a graft from a mismatched donor, comprising:

reactivating the thymus of the patient; and

administering cells having the same histocompatibility as

that of the mismatched donor to the patient, the cells being selected

from the group consisting of stem cells, progenitor cells, dendritic cells,

and combinations thereof,

wherein the patient has an increased tolerance to the graft compared to an untreated patient.

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Claim 68. (Previously Presented): The method of claim 66, wherein the cells administered to the patient are from the mismatched donor.

Claim 69. (Currently Amended): A method for inducing increasing tolerance in a patient to a graft from a MHC-mismatched donor, comprising:

providing the patient with immunosuppressive therapy;

reactivating the thymus of the patient; [[and]]

administering cells having the same histocompatibility as that of the MHC-mismatched donor to the patient, the cells being selected from the group consisting of stem cells, progenitor cells, dendritic cells, and combinations thereof[[,]]; and

providing the graft from the MHC-mismatched donor to the patient,

wherein the patient has an increased tolerance to the graft compared to an untreated patient.

Claim 70. (Previously Presented): The method of claim 69, wherein the cells administered to the patient are from the mismatched donor.

Claim 71. (Withdrawn-Currently Amended): The method of claim 35, wherein the anti-androgen is flutamide EULEXINTM or ketoconazole.

Claim 72. (Withdrawn): The method of claims 19 or 53, wherein the donor is xenogeneic to the patient.

Claim 73. (Withdrawn): A method for inducing tolerance in a patient to a graft from a xenogeneic donor, comprising:

reactivating the thymus of the patient; and

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administering cells from the xenogeneic donor to the patient, the cells
being selected from the group consisting of stem cells, progenitor cells,
dendritic cells, and combinations thereof,
wherein the patient has an increased tolerance to the graft compared to an untreated
patient.

Claim 74. (Withdrawn): A method for inducing tolerance in a patient to a graft from a
xenogeneic donor, comprising:

depleting T cells of the patient;
reactivating the thymus of the patient; and
administering cells from the xenogeneic donor to the patient, the cells
being selected from the group consisting of stem cells, progenitor cells,
dendritic cells, and combinations thereof,
wherein the patient has an increased tolerance to the graft compared to an untreated
patient.

Claim 75. (Withdrawn): A method for inducing tolerance in a patient to a graft from a
xenogeneic donor, comprising:

depleting T cells of the patient;
reactivating the thymus of the patient; and
administering cells having the same histocompatibility as
that of the xenogeneic donor to the patient, the cells being selected from
the group consisting of stem cells, progenitor cells, dendritic cells, and
combinations thereof,
wherein the patient has an increased tolerance to the graft compared to an untreated
patient.